

CLAIMS

Please amend the presently pending claims as follows:

1. **(Currently Amended)** A method of selectively inhibiting expression of a mutant target allele of a gene in a cell or organism comprising wild-type and mutant alleles of the gene, wherein the target allele comprises a dominant gain of function mutation that is correlated with a neurodegenerative disorder associated with a mutant protein encoded by the mutant allele, the mutant protein having a toxic property, the method comprising administering to the cell or organism an siRNA specific for the target allele such that allele-specific RNA interference of the mutant target allele occurs and expression of the wild-type allele is preserved.
2. **(Cancel)**
3. **(Currently Amended)** The method of claim 1~~or 9~~2, wherein the neurodegenerative disorder is selected from the group of amyotrophic lateral sclerosis, Huntington's disease, Alzheimer's disease, and Parkinson's disease.
4. **(Currently Amended)** The method of claim 1~~2~~, wherein the neurodegenerative disorder is amyotrophic lateral sclerosis.
5. **(Previously Presented)** The method of claim 1, wherein the siRNA is targeted to the gain of function mutation.
6. **(Previously Presented)** The method of claim 1, wherein the siRNA is capable of single nucleotide discrimination.
7. **(Previously Presented)** The method of claim 1, wherein the mutant and wild-type alleles differ by only one, two, or three nucleotides.

8. **(Previously Presented)** The method of claim 1, wherein the mutant and wild-type alleles differ by only a single nucleotide.
9. **(Currently Amended)** A method of selectively inhibiting expression of a mutant target allele of a gene in a cell or organism comprising wild-type and mutant alleles of the gene, wherein the mutant target allele comprises a point mutation correlated with a dominant gain-of-function neurodegenerative disorder associated with a mutant protein encoded by the mutant allele, the mutant protein having a toxic property, the method comprising administering to the cell or organism an siRNA targeted to the point mutation such that allele-specific RNA interference of the mutant target allele occurs and expression of the wild-type allele is preserved.
10. **(Cancel)**
11. **(Previously Presented)** The method of claim 9, where the siRNA is capable of single nucleotide discrimination.
12. **(Previously Presented)** The method of claim 9, wherein the mutant and wild-type alleles differ by one, two, or three nucleotides.
13. -27. **(Canceled)**
28. **(Previously Presented)** The method of claim 9, wherein the mutant and wild-type alleles differ by a single nucleotide.
29. **(Currently Amended)** The method of claim 1 or 9, wherein the siRNA is matched completely with a mutant mRNA encoded by the mutant allele ~~point mutation~~ but comprises a single nucleotide mismatch with a wild-type mRNA encoded by the wild-type allele.
30. **(Previously Presented)** The method of claim 29, wherein the mismatch is a purine:purine mismatch.

31. **(Previously Presented)** The method of claim 30, wherein the mismatch is a G:G mismatch.
32. **(Previously Presented)** The method of claim 29, wherein the single nucleotide mismatch is located at nucleotide position 10 (P10) relative to the 5' end of the antisense strand of the siRNA.
33. **(Previously Presented)** The method of claim 29, wherein the single nucleotide mismatch is located at nucleotide position 9 (P9) relative to the 5' end of the antisense strand of the siRNA.
34. **(Cancel)**
35. **(Currently Amended)** The method of claim ~~23~~4, wherein the neurodegenerative disorder is amyotrophic lateral sclerosis.
36. **(Previously Presented)** The method of claim 35, wherein the gene is SOD1.
37. **(Previously Presented)** The method of claim 36, wherein the mutant allele encodes a glycine to arginine mutation at amino acid position 85 (G85R) of a SOD1 protein.
38. **(Previously Presented)** The method of claim 36, wherein the mutant allele encodes a glycine to alanine mutation at amino acid position 93 (G93A) of a SOD1 protein.
39. **(Previously Presented)** The method of claim 36, wherein the siRNA comprises (i) a sense strand sequence corresponding to the sequence set forth as SEQ ID NO: 3; and (ii) an anti-sense strand sequence set forth as SEQ ID NO: 4.
40. **(Previously Presented)** The method of claim 36, wherein the siRNA comprises (i) a sense strand sequence set forth as SEQ ID NO: 1; and (ii) an anti-sense strand sequence set forth as SEQ ID NO: 2.

41. **(Previously Presented)** The method of claim 1 or 9, wherein the siRNA is administered to cell in the form of a shRNA, wherein the shRNA is cleaved in the cell to generate the siRNA.
42. **(Previously Presented)** The method of claim 41, wherein the shRNA is matched with a mutant mRNA encoded by the mutant allele and contains a single nucleotide mismatch with a wild-type mRNA encoded by the wild-type allele.
43. **(Previously Presented)** The method of claim 42, wherein the single nucleotide mismatch is located at position (P10) relative to the 5' end of the shRNA.
44. **(Previously Presented)** The method of claim 43, wherein the gene is SOD1.
45. **(Previously Presented)** The method of claim 44, wherein the shRNA is a G93A SOD1 shRNA.
46. **(Previously Presented)** The method of claim 45, wherein the G93A SOD1 shRNA has the sequence set forth as SEQ ID NO: 16.
47. **(Previously Presented)** The method of claim 41, wherein the shRNA is expressed from an expression construct.
48. **(Previously Presented)** The method of claim 47, wherein the shRNA is expressed under the control of a RNA polymerase III (U6) promoter.